

Claims

1. A polypeptide comprising the amino acid sequence shown in SEQ ID
5 NO: 2, 4, or 6.
2. A polypeptide claimed in Claim 1 which is an oxidase which is
capable to produce H_2O_2 .
- 10 3. A polypeptide as claimed in any one of the Claims 1 to 2 which is
an alpha amino acid oxidase.
4. A polypeptide as claimed in Claim 3 which is a L-lysine and/or L
arginine oxidase.
- 15 5. A polypeptide comprising a fragment of the polypeptide as claimed
in any one of the Claims 1 to 4.
6. A polypeptide as claimed in Claim 5 which is obtained by protease
20 digestion of the polypeptide as claimed in any of the Claims 1 to 4.
7. A polypeptide as claimed in Claim 6 which is obtained by proteinase
K digestion.
- 25 8. A polypeptide as claimed in Claim 5 comprising the sequence
selected from amino acid residue No. 39 to 77 in SEQ ID NO: 2.
9. A polypeptide as claimed in Claim 8 comprising 1 to 20 additional
amino acid residues at the N-terminus and/or the C-terminus
30 selected from the sequences of SEQ ID NO: 2 or SEQ ID NO: 4
adjacent to the sequence selected in claim 8.

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10. A polypeptide as claimed in Claim 8 comprising 1 to 10 additional amino acid residues at the N-terminus and/or the C-terminus selected from the sequences of SEQ ID NO: 2 adjacent to the sequence selected in claim 8.

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11. A polypeptide as claimed in Claim 8 comprising 1 to 5 additional amino acid residues at the N-terminus and/or the C-terminus selected from the sequences of SEQ ID NO: 2 adjacent to the sequence selected in claim 8.

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12. A polypeptide as claimed in any one of the Claims 2 to 11, wherein the H₂O₂ producing activity can be regulated by the addition or removal of an L-amino acid.

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13. A polypeptide as claimed in Claim 12 which is regulated by L-lysine, L-arginine, a derivative or precursor of L-lysine, a derivative or a precursor of L-arginine, or a mixture thereof.

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14. A polypeptide which has an identity to the polypeptides of any of the claims 1 to 13 of at least 70%.

15. A polypeptide as claimed in any one of the claims 1 to 14 which is a recombinant polypeptide.

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16. The polypeptide as claimed in claim 15, which is a fusion polypeptide.

17. A nucleic acid encoding a polypeptide of any of the Claims 1 to 16.

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18. The nucleic acid of Claim 17 comprising

(a) a nucleotide sequence as shown in SEQ ID NO: 1, 3, or 5, or at least the polypeptide coding portion thereof, or the complement thereof, or

(b) a nucleotide sequence corresponding to the sequence of (a) within the scope of degeneracy of the genetic code, or the complement thereof, or

(c) a nucleotide sequence hybridizing under stringent condition with the sequence of (a) and/or (b), or

(d) a nucleotide sequence which has a homology of at least 70% to the sequences of (a) and/or (b).

19. The nucleic acid of claim 17 or 18 operatively linked to an expression control sequence.

20. The nucleic acid of any one of claims 17 to 19 which is a recombinant vector.

21. A recombinant cell comprising the nucleic acid of any one of the Claims 17 to 20.

22. An antibody directed against a polypeptide of any one of the Claims 1 to 16.

23. A pharmaceutical composition or a kit of pharmaceutical compositions comprising the polypeptide as claimed in any of the Claims 1 to 16, in a pharmaceutically effective amount and optionally together with suitable diluents, carriers and/or adjuvants.

24. The pharmaceutical composition or kit of Claim 23 comprising at least one further component which is a substance capable of modulating the cytotoxic activity of the polypeptide.

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25. The pharmaceutical composition or kit of Claim 24, wherein the polypeptide and the modulating substances are provided as separate preparations.
- 5 26. The pharmaceutical composition or kit of Claim 25, wherein the polypeptide is provided for administration before the modulating substances.
- 10 27. The pharmaceutical composition or kit of any one of the Claims 24 to 26, wherein the modulating substance selected from (i) L-lysine, L-arginine, a derivative or precursor of L-lysine, a derivative or precursor of L-arginine, or a mixture thereof, and/or (ii) a flavine nucleoside.
- 15 28. The pharmaceutical composition or kit of any one of the Claims 24 to 27, further comprising a nucleic acid, and/or a recombinant cell, and/or an APIT inhibitor.
- 20 29. The pharmaceutical composition or kit of Claim 28, wherein the inhibitor is an antibody against the polypeptide.
30. A polypeptide, and/or a nucleic acid, and/or a recombinant cell, and/or an inhibitor as claimed in any one of the Claims 1 to 22, for use in a diagnostic or therapeutic method in humans or animals.
- 25 31. A polypeptide, and/or a nucleic acid, and/or a recombinant cell, and/or an inhibitor as claimed in Claim 30 for diagnosis or treatment of cancer.
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32. A polypeptide, and/or a nucleic acid, and/or a recombinant cell, and/or an inhibitor as claimed in Claim 30 or 31 for diagnosis or treatment of lung cancer, breast cancer, prostate cancer, colon cancer, cervix cancer, uterus cancer, larynx cancer, stomach cancer, liver cancer, Ewings sarkoma, acute lymphoid leukemia, chronic myeloid leukemia, apoptosis resistant leukemia, MDR lung cancer, pancreas cancer, gastric cancer, kidney cancer, gliomas, melanomas, chronic lymphoid leukemia, and/or lymphoma.

33. Use of a substance as described in Table 3 or/and Table 4 or/and Table 5 as target substance for a polypeptide of any one of Claim 1-16.

34. Use of claim 33 in which the target substance is a protein.

35. Use of claim 34 in which the target substance is a peroxidase, particularly peroxiredoxin I.

36. Use of claim 35 in which the target substance comprises

- (a) the amino acid sequence shown in SEQ ID NO: 8, or/and
- (b) an amino acid sequence which is homologous to the sequence of (a) with at least 70%, or/and
- (c) a fragment of the amino acid sequence of (a) or (b).

37. Use of claim 33 in which the target substance is a nucleic acid.

38. Use of claim 37 in which the target substance codes for a peroxidase, particularly peroxiredoxin I.

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39. Use of claim 38 in which the target substance comprises
- (a) the nucleotide sequence shown in SEQ ID NO: 7, or/and
 - (b) a nucleotide sequence which corresponds to the sequence of (a) within the scope of the degeneracy of the genetic code, or/and
 - (c) a nucleotide sequence hybridizing to the sequence of (a) or/and (b) under stringent conditions, or/and
 - (d) a fragment of the nucleotide sequence of (a), (b) or (c).
40. Use of a substance of any one of the claims 33 to 39 for the identification of new pharmaceutical agents, particularly in a screening method.
41. A pharmaceutical composition or kit comprising as an active agent a combination of APIT and at least one inhibitor of a substance of any one of claims 33 to 39.
42. An inhibitor of peroxiredoxin I activity which is an RNA molecule, particularly a double stranded RNA molecule comprising a nucleic acid of at least 15 nucleotides complementary to a peroxiredoxin I transcript.
43. An inhibitor as claimed in claim 42, wherein the peroxiredoxin I transcript is derived from the sequence of SEQ ID NO: 7.
44. An inhibitor as claimed in claims 42 or 43, wherein the one or two strands independently have a length of 19 to 25 nucleotides, preferably 19 to 23 nucleotides.

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45. An inhibitor as claimed in any of the claims 42 to 44 which is a double-stranded RNA molecule having a sequence selected from the group of sequences consisting of SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11; SEQ ID NO: 12; SEQ ID NO: 13; SEQ ID NO: 14; SEQ ID NO: 15; SEQ ID NO: 16; SEQ ID NO: 17; SEQ ID NO: 18; SEQ ID NO: 19; SEQ ID NO: 20; SEQ ID NO: 21; SEQ ID NO: 22; SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29, optionally with one or two 3' overhangs and optionally one or more modified nucleotides.
46. A pharmaceutical composition or kit comprising an inhibitor or a nucleic acid encoding an inhibitor as claimed in any one of the claims 42 to 45.
47. A pharmaceutical composition as claimed in claim 46, comprising a gene therapy delivery system suitable for the delivery of a nucleic acid encoding the inhibitor as claimed in any of the claims 42 to 45 to predetermined tissues or/and cell types.
48. Use of an inhibitor as claimed in any of the claims 42 to 45 for the manufacture of a medicament for the diagnosis or/and treatment of cancer.
49. A pharmaceutical composition or kit comprising
- (I) a polypeptide obtainable from *Aplysia*, comprising an amino acid sequence selected from:
 - (a) D-G-E-D-A-A-V (SEQ ID NO:32) and/or
 - (b) (D/Q)-G-(I/V)-C-R-N-(Q/R)-R-(Q/P) (SEQ ID NO:33),
 - (c) F-A-D-S (SEQ ID NO:34),
 - (d) G-P-D-G-(I/L)-V-A-D (SEQ ID NO:35),
 - (e) P-G-E-V-S-(K/Q)-(I/L) (SEQ ID NO: 36),

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- (f) A-T-Q-A-Y-A-A-V-R-P-I-P-A-S-K (SEQ ID NO:37),
- (g) D-S-G-L-D-I-A-V-E-Y-S-D-R (SEQ ID NO:38),
- (h) G-D-V-P-Y-D-L-S-P-E-E-K (SEQ ID NO: 39) or/and
- (i) SEQ ID NO: 41, 43, 44, 45.

5 or a fragment thereof,

wherein the polypeptide or fragment has cytotoxic activity,
or/and a nucleic acid comprising

- (i) a nucleotide sequence as shown in SEQ ID NO: 40 or
42 or at least the polypeptide coding portion thereof or
10 the complement thereof,
- (ii) a nucleotide sequence corresponding to the sequence
of (i) within the scope of degeneracy of the genetic
code, or the complement thereof, or/and
- (iii) a nucleotide sequence hybridizing under stringent
15 conditions with the sequence of (i) or/and (ii), and

(II) an inhibitor of a target substance as described in Table 3
or/and Table 4 or/and Table 5.

50. A method for the diagnosis or treatment of cancer, wherein the
20 pharmaceutical composition or kit as claimed in claims 41, 46, 47 or
49 is administered to a subject in need thereof.